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22. (Amended) The method of claim 19, wherein said sample comprises human hemoglobin or a blood substitute.

23. (Amended) A method of determining a level of alkaline phosphatase in a sample, comprising:

measuring a first change in absorbance of said sample at 450 ± 10 nm;

adding 4-nitrophenyl phosphate to said sample;

measuring a second change in absorbance of said sample at 450 ± 10 nm;

and

correcting the first change in absorbance with the second change in absorbance.

REMARKS

Applicants submit this Reply and Amendment in response the Examiner's Office Action mailed on October 28, 2002, setting a shortened statutory period for response of three months. A petition to extend that period by three months is submitted herewith. In the subject Office Action, the Examiner provisionally rejected claims 8-24 under the judicially created doctrine of obviousness-type double patenting over the claims of copending application number 09/807,079. The Examiner also objected to the specification for informalities, and rejected claims 8-24 under 35 U.S.C. §102(a). Lastly, the Examiner rejected claims 8-15 and 17-24 under 35 U.S.C. §102(b).

1. Rejection of claims under the judicially created doctrine of obviousness-type double patenting

The Examiner provisionally rejected claims 8-24 over the claims of copending application 09/807,079 (the '079 application) for obviousness-type double patenting.

Specifically, the Examiner indicated that claims 8-24 of the present application are not patentably distinct from claims 12-29 of the '079 application. Applicants respectfully traverse this provisional rejection, and assert that the claims of the present and '079 applications define patentably distinct inventions.

These two applications are similar to the extent that both are directed to methods of eliminating interference by hemoglobin in the determination of alkaline phosphatase. The methods of these two applications, however, represent distinctly different approaches to solving the problem of hemoglobin interference.

Methods according to the '079 application use an optical measurement taken at 450 ±10 nm in combination with an optical measurement taken at a secondary wavelength. All claims of the '079 application require two optical measurements taken at different wavelengths. Further, all claims of the '079 application require combining the two measurements, and do not require any correlation with a degree of hemoglobin in the sample, as required by all claims of the present application. The claims of the current application require taking an optical measurement at 450 ± 10 nm and correcting the measurement with a correlation between the degree of hemoglobin of a sample with a level of interference due to the presence of hemoglobin.

Furthermore, considering the claims of the '079 application, it would not have been obvious to one of ordinary skill in the art to arrive at the invention defined by the claims of the present application. As discussed above, the '079 application does not utilize the presently claimed method, but rather uses measurements at multiple wavelengths. With the claims of the '079 application in hand, a skilled artisan would not be motivated to produce the invention claimed in the present application because, as indicated in the '079 application, the method of the '079 application produces a complete elimination of interference. Practicing this method, the skilled artisan would have no technological motivation to use other means for eliminating such interference.

Accordingly, Applicants respectfully traverse the Examiner's provisional rejection of claims 8-24 of the present application under the judicially created doctrine of obviousness-type double patenting and request withdrawal of this provisional rejection.

2. Objections to the specification for informalities

The Examiner objected to the specification because the various sections were not labeled or separated by headings, claims 22 and 23 were misnumbered, and the first sentence of Example b) lacked a period. Applicants herein amend the current specification by inserting various heading paragraphs and adding a period to the first sentence of Example b). Also, applicants gratefully acknowledge the Examiner's correction of the typographical error in the numbering of the claims and do not object to the correction entered by the Examiner. Applicants believe that the amendments made herein overcome all of the Examiner's objections to the specification.

3. Rejection of claims under 35 U.S.C. §102(a)

The Examiner rejected claims 8-24 under 35 U.S.C. §102(a) as being anticipated by US patent 6,013,467 to Siedel et al. for Blood Substitute Suppression by Peroxides (the '467 patent). The Examiner indicated that the rejection was based on the '467 patent, but also detailed the relationship between the '467 patent and WO 98/02570 (the Siedel PCT). While the Applicants are willing to use the text of the '467 patent to discuss the rejection to the extent it is identical to the Siedel PCT, they respectfully assert that the rejection cannot be based on the '467 patent because the '467 patent is not prior art to the present application. The Applicants discuss this rejection below as if it had been entered as a rejection based on the Siedel PCT and use the '467 patent simply as an English language version of this reference. Applicants take this approach to facilitate prosecution, and do not thereby make any admission or acknowledgement that the '467 patent constitutes prior art to the claims of the present application.

To properly support a rejection under 35 U.S.C. §102, a reference must disclose each and every limitation of the rejected claim. The independent claims of the present application define a rate-blank method, i.e., measuring an optical change at 450 nm before and after the main reaction started by adding 4-nitrophenyl phosphate to the sample. Also, the second optical measurement, i.e., the measurement determined after the main reaction, is corrected by the first optical measurement, i.e., the measurement determined

before the main reaction. The first optical measurement correlates with the level of interference due to hemoglobin.

The '467 patent does not disclose such a step or correlation factor. The methods of the '467 patent rely solely on peroxide reagents to bleach out any interfering color due to the presence of hemoglobin, and do not utilize any type of rate-blank method. Indeed, a thorough review of the '467 patent reveals a complete lack of any disclosure of absorbance change measurements that represent a correlation between the hemoglobin in a sample and the level of interference due to hemoglobin. As a result, the '467 patent cannot properly serve as a basis for rejection under 35 U.S.C. §102.

Accordingly, the Examiner's §102 rejection of claims 8-24 based on the Siedel PCT is improper and should be withdrawn.

4. Rejection of claims under 35 U.S.C. §102(b)

The Examiner rejected claims 8-15 and 17-24 under 35 U.S.C. §102(b) as being anticipated by US 6,207,459 to Weisheit et al. for a Method for the Analysis of Medical Samples Containing Haemoglobin (the '459 patent). The Examiner indicated that the rejection was based on the '459 patent, but also detailed the relationship between the '459 patent and WO 97/45732 (the Weisheit PCT). As with the Siedel et al. reference, Applicants are willing to use the text of the '459 patent to discuss the rejection to the extent it is identical to the Weisheit PCT. Nevertheless, the rejection cannot be properly based on the '459 patent because the '459 patent is not prior art to the present application. The Applicants discuss this rejection below as if it had been entered as a rejection based on the Weisheit PCT and use the '459 patent simply as an English language version of this reference. Applicants take this approach to facilitate prosecution, and do not thereby make any admission or acknowledgement that the '459 patent constitutes prior art to the claims of the present application.

As noted, above, the independent claims of the present application require a rate-blank method, which involves measuring the change in absorbance at 450 nm before and after the main reaction, which is initiated by adding 4-nitrophenyl phosphate to the sample. Also, the method requires correcting the optical measurement determined after the main

reaction with the optical measurement determined before the main reaction. The optical measurement determined before the main reaction correlates with the level of interference due to hemoglobin.

The '459 patent is devoid of any disclosure of a primary measurement wavelength of 450 nm. Rather, it discloses a method to correct an analyte value measured in a sample containing hemoglobin. This method is complex, requiring five steps as well as an additional experimental determination of the test specific correction factor. Furthermore, a thorough review of the '459 patent reveals a complete lack of any disclosure of rate-blank methods, such as the use of absorbance change measurements that represent a correlation between the degree of hemoglobin of a sample and the level of interference due to hemoglobin. Thus, the '459 patent cannot properly serve as a basis for rejection under §102.

CONCLUSION

In light of the above, Applicants have overcome each and every one of the Examiner's objections and rejections. The application is therefore in condition for allowance on the next office action. If, however, the Examiner feels that personal communication would facilitate the prosecution of this case, applicants request that the Examiner contact their attorney at the number listed below.

Respectfully submitted,

Dated: April 28, 2003

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Appendix A

Determination according to the recommendation to the Société Francaise de Biologie Clinique according to Ann. Biol. Clin. Vol. 35, 271 (1977).

Appendix B

8. (Amended) A method of eliminating interference by hemoglobin in the determination of alkaline phosphatase in a sample, comprising:

[determining a degree of hemolysis of said sample];

determining [an] a first optical measurement of said sample at 450 ± 10 nm

adding 4-nitrophenyl phosphate to said sample;

determining [an] a second optical measurement of said sample at 450 ± 10 nm;

[determining a correction factor by correlating the degree of hemolysis of said sample with a level of interference due to said hemoglobin;] and

correcting the second optical measurement [by combining] with the [correction factor with the] first optical measurement.

16. (amended) The method of claim 8, wherein the step of determining [an] a first optical measurement is conducted over a period of time of between about 1 and 4 minutes.

19. (new) A method of determining a level of alkaline phosphatase in a sample [containing 4-nitrophenyl phosphate], the method comprising:

determining [an] a first optical measurement of said sample at 450 ± 10 nm that represents a correlation between the amount of hemoglobin in the sample and the interference due to the hemoglobin; and

adding 4-nitrophenyl phosphate to said sample;

determining a second optical measurement of said sample at 450 ± 10 nm;

correcting the second optical measurement [by] with [combining] the first optical measurement [with a correction factor that represents a correlation between a degree of hemolysis of said sample and a level of interference due to hemoglobin present in said sample].

20. (Amended) The method of claim 19, wherein the [correction factor] first optical measurement is determined in a pre-reaction.

22. (Amended) The method of claim 19, wherein said sample comprises human hemoglobin or a blood substitute.

23. (Amended) A method of determining a level of alkaline phosphatase in a sample, comprising:

[determining a degree of hemolysis of said sample;]

measuring a first change in absorbance of said sample at 450 ± 10 nm;

adding 4-nitrophenyl phosphate to said sample;

measuring a second change in absorbance of said sample at 450 ± 10 nm;

[determining a correction factor by correlating the degree of hemolysis of said sample with a level of interference due to hemoglobin which may be present in said sample]; and

correcting the first change in absorbance [by combining] with the second change in absorbance [with the correction factor].